Docket No.: ISIS-5297

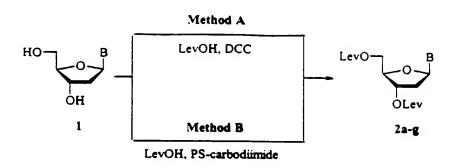
App No.: Not Yet Assigned Filed: Herewith

Title: BUILDING BLOCKS FOR THE SOLUTION PHASE SYNTHESIS OF
OLIGONUCLEOTIDES
Inventors: Yogesh S. Sanghvi; Vincente Goto; Miguel Ferrero; Susana Fernandez; Javier E.
Garcia

Attorney: Jeffrey H. Rosedale Phone: (215) 568-3100

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a, B= T; b, B= C; c, B= C^{Bz} ; d, B= A; e, B= A^{Bz} ; f, B= G; g, B= G^{Bu}

Method A: LevOH, DCC, DMAP, Et₃N, 1,4-Dioxane.

Method B: LevOH, PS-carbodiimide, DMAP, DMAP•HCl, Et₃N, 1,4-Dioxane.

PS-carbodiimide

FIGURE 1

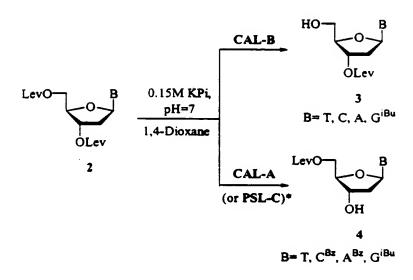
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*PSL-C was used for di-Lev-dGiBu (2g) since CAL-A did not catalyze the hydrolysis.

FIGURE 2

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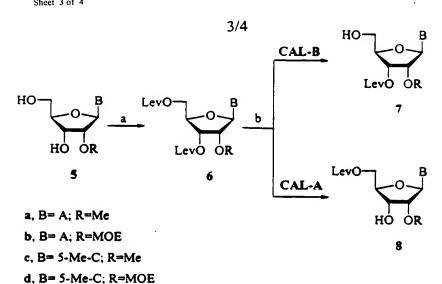
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- (a) LevOH, DCC, Et₃N, DMAP, 1,4-dioxane.
- (b) 0.15M KPi (pH=7), 1,4-dioxane.

FIGURE 3

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Table 1. Regioselective Enzymatic Hydrolysis of di-Levulinyl esters 2.

entry	substrate	enzyme	T (°C)	<i>t</i> (h)	Yield (%)	
					3	4
1	2 a	CAL-B	40	62	85	
2	2 b	CAL-B	30	62	84	
3	2 d	CAL-B	40	28	98	
4	2 g	CAL-B	40	18	80	
5	2a	CAL-A	40	86		70
6	2e	CAL-A	40	62		78
7	2e	CAL-A	40	68		85
8	2g	PSL-C	60	28		93

a Isolated yield.

b An extra fraction of lipase (30 mg) was added after 30 h.

^c It was used a ratio of 1:2 w/w (2g/CAL-B).

a. B= T; b, B= C; c, B= C^{Bz} ; d, B= A; e, B= A^{Bz} ; f, B= G; g, B= G^{iBu}